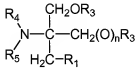
Claims

1. (Currently Amended) A method of treating an individual in need of treatment for a vascular permeability disorder, comprising administering to the individual in need of treatment for a vascular permeability disorder a therapeutically effective amount of ~~The use of~~ a vascular endothelial sphingosine-1-phosphate receptor agonist~~, a pharmaceutically acceptable form thereof, or a phosphorylated form thereof, for the manufacture of a medicament for the treatment of a vascular permeability disorder~~, wherein the vascular endothelial sphingosine-1-phosphate receptor agonist is not sphingosine-1-phosphate.

2. (Currently Amended) The method~~use~~ of Claim 1, wherein the vascular endothelial sphingosine-1-phosphate receptor agonist is a 1,2-aminoalcohol, a pharmaceutically acceptable salt thereof, or a phosphorylated form thereof, having the formula



wherein R_1 is a substituted or unsubstituted straight- or branched carbon chain having 12 to 22 carbon atoms, and each of R_2, R_3, R_4 and R_5 are independently hydrogen or lower alkyl.

3. (Currently Amended) The method~~use~~ of Claim 2, wherein R_1 is interrupted by a substituted or unsubstituted phenylene.

4. (Currently Amended) The method~~use~~ of Claim 3, wherein the vascular endothelial sphingosine-1-phosphate receptor agonist is 2-amino-2-[2-(4-octaphenyl)ethyl]propane-1,3 diol, 2-amino-2-methyl-4-[4-heptoxy-phenyl]butane-1-ol, 2-amino-3-phosphate-2-[2-4-octaphenyl)ethyl]propane-1-ol, 2-amino-2-methyl-4-[4-heptoxy-phenyl]1-diphosphoric acid, or a combination comprising one or more of the foregoing agoniststs.

5. (Currently Amended) The method~~use~~ of Claim 1, wherein the vascular endothelial sphingosine-1-phosphate receptor agonist is phosphorylated by sphingosine kinase-2.

6. (Currently Amended) The ~~method~~use of Claim 1, wherein the vascular endothelial sphingosine-1-phosphate receptor agonist stimulates phosphorylation of an Akt protein kinase, an ERK protein kinase, or a combination comprising one or more of the foregoing kinases.

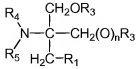
7. (Currently Amended) The ~~method~~use of Claim 1, wherein the vascular endothelial sphingosine-1-phosphate receptor is $S1P_1$, $S1P_2$, $S1P_3$, $S1P_4$, $S1P_5$, or a combination comprising one or more of the foregoing receptors.

8. (Currently Amended) The ~~method~~use of Claim 7, wherein the vascular endothelial sphingosine-1-phosphate receptor agonist induces adherens junction assembly.

9. (Currently Amended) The ~~method~~use of Claim 1, wherein the vascular permeability disorder is endothelial injury, thrombocytopenia, atherosclerosis, ischemic cardiovascular disease, ischemic peripheral vascular disease, a peripheral vascular disorder associated with diabetes, Dengue hemorrhagic fever, adult (acute) respiratory distress syndrome, vascular leak syndrome, sepsis, autoimmune vasculitis, or a combination comprising one or more of the foregoing disorders.

10. (Currently Amended) A method of treating an individual in need of treatment for unwanted vascular endothelial cell apoptosis, comprising administering to the individual in need of treatment for unwanted vascular endothelial cell apoptosis a therapeutically effective amount of ~~The use of~~ a vascular endothelial sphingosine-1-phosphate receptor agonist, a pharmaceutically acceptable form thereof, or a phosphorylated form thereof~~, for the manufacture of a medicament for the treatment of unwanted vascular endothelial cell apoptosis~~, wherein the vascular endothelial sphingosine-1-phosphate receptor agonist is not sphingosine-1-phosphate, and wherein the unwanted vascular endothelial cell apoptosis is not related to transplant rejection.

11. (Currently Amended) The methoduse of Claim 10, wherein the vascular endothelial sphingosine-1-phosphate receptor agonist is a 1,2-aminoalcohol, a pharmaceutically acceptable salt thereof, or a phosphorylated form thereof, having the formula



wherein R_1 is a substituted or unsubstituted straight- or branched carbon chain having 12 to 22 carbon atoms, and each of R_2, R_3, R_4 and R_5 are independently hydrogen or lower alkyl.

12. (Currently Amended) The methoduse of Claim 11, wherein R_1 is interrupted by a substituted or unsubstituted phenylene.

13. (Currently Amended) The methoduse of Claim 12, wherein the vascular endothelial sphingosine-1-phosphate receptor agonist is 2-amino-2-[2-(4-octaphenyl)ethyl]propane-1,3 diol, 2-amino-2-methyl-4-[4-heptoxy-phenyl]butane-1-ol, 2-amino-3-phosphate-2-[2-4-octaphenyl)ethyl]propane-1-ol, 2-amino-2-methyl-4-[4-heptoxy-phenyl]1-diphosphoric acid, or a combination comprising one or more of the foregoing agonists.

14. (Currently Amended) The methoduse of Claim 12, wherein the vascular endothelial sphingosine-1-phosphate receptor agonist is phosphorylated by sphingosine kinase-2.

15. (Currently Amended) The methoduse of Claim 12, wherein the vascular endothelial sphingosine-1-phosphate receptor agonist stimulates phosphorylation of an Akt protein kinase, an ERK protein kinase, or a combination comprising one or more of the foregoing kinases.

16. (Currently Amended) The methoduse of Claim 10, wherein the vascular endothelial sphingosine-1-phosphate receptor is $S1P_1$, $S1P_2$, $S1P_3$, $S1P_4$, $S1P_5$, or a combination comprising one or more of the foregoing receptors.

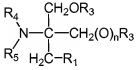
17. (Currently Amended) The methoduse of Claim 10, wherein the unwanted vascular endothelial cell apoptosis is related to an apoptosis-related disorder.

18. (Currently Amended) The methoduse of Claim 17, wherein the apoptosis-related disorder is idiopathic cardiomyopathy, cardiomyopathy induced by drugs, cardiomyopathy induced by chronic alcoholism, familial cardiomyopathy, viral myocarditis, viral cardiomyopathy, cardiac infarction, cardiac angina, peripheral thrombosis, congestive heart failure, arrhythmia, cerebral stroke, subarachnoidal hemorrhage, cerebral infarction, cerebral thrombosis, or a combination comprising one or more of the foregoing disorders.

19. (Currently Amended) The methoduse of Claim 10, wherein the unwanted vascular endothelial cell apoptosis is associated with radiation therapy.

20. (Currently Amended) A method of treating a mammal in need of stimulation of new blood vessel formation, comprising administering to the mammal in need of stimulation of new blood vessel formation a therapeutically effective amount of ~~The use of~~ a vascular endothelial sphingosine-1-phosphate receptor agonist, a pharmaceutically acceptable form thereof, or a phosphorylated form thereof~~, for the manufacture of a medicament for the stimulation of new blood vessel formation in a mammal~~, wherein the vascular endothelial sphingosine-1-phosphate receptor agonist is not sphingosine-1-phosphate.

21. (Currently Amended) The methoduse of Claim 20, wherein the vascular endothelial sphingosine-1-phosphate receptor agonist is a 1,2-aminoalcohol, a pharmaceutically acceptable salt thereof, or a phosphorylated form thereof, having the formula



wherein R_1 is a substituted or unsubstituted straight- or branched carbon chain having 12 to 22 carbon atoms, and each of R_2, R_3, R_4 and R_5 are independently hydrogen or lower alkyl.